

What is claimed is:

1. An assay for diagnosing whether a subject has or is predisposed to developing a neoplastic disease which comprises:
- a) obtaining a biological sample from a first subject;
  - b) contacting the sample with an agent capable of detecting the amount of soluble neuregulin receptor in the sample;
  - c) measuring the amount of agent bound by the sample;
  - d) comparing the amount of agent bound measured in step c) with the the amount of agent bound by a sample which is from a second subject without neoplastic disease, a higher amount bound by the sample from the first subject being indicative of the first subject having or being predisposed to developing a neoplastic disease.
2. An assay for determining whether a subject has a neurodegenerative disease which comprises:
- a) obtaining a biological sample from the subject;
  - b) contacting the sample with an agent that detects the presence of an extracellular domain of nARIA (CRD-neuregulin) or an agent which detects the presence of soluble neuregulin receptor;
  - c) measuring the amount of agent bound by the sample;
  - d) comparing the amount of bound agent measured in step c) with the the amount of agent bound by a standard normal sample, a higher amount or a lower amount bound by the sample from the subject being indicative of the subject having a neurodegenerative disease.

3. The assay of claim 1 or 2, wherein the agent is an antibody or a fragment thereof, a cell which expresses neuregulin which has a cytoplasmic tail linked to a detectable label; or a cell which expresses neuregulin receptor.  
5
4. The assay of claim 1 or 2, wherein the sample is cerebrospinal fluid (CSF), blood, plasma, sputum, amniotic fluid, ascites fluid, breast aspirate, saliva,  
10 urine, lung lavage, or cell lysate or extract derived from a biopsy.
5. The assay of claim 1 or 2, wherein sample further comprises soluble her 4 receptor.  
15
6. The assay of claim 1 or 2, wherein the agent is an antibody which binds to an epitope of the cytoplasmic domain of nARIA.
- 20 7. The assay of claim 1 or 2, wherein the agent is a HEK cell stably transfected with neuregulin with a cytoplasmic tail detectably labelled.
8. The assay of claim 1, wherein the neoplastic disease is breast cancer, prostate cancer, brain cancer or ovarian cancer.  
25
9. The assay of claim 2, wherein the neurodegenerative disease is Alzheimer's Disease, Parkinson's disease,  
30 Turrets Syndrome, amyotrophic lateral sclerosis, Pick's disease, myasthenia gravis, or senility.
10. A method for maintaining or sustaining a synaptic connection between a neuron and a target cell  
35 comprising contacting the target cell with an nARIA

polypeptide or a nucleic acid molecule encoding nARIA or biologically active variant thereof, in an amount sufficient to maintain the synaptic connection.

- 5     11. A method for treating neurodegeneration in a subject comprising contacting the target cell with an nARIA polypeptide or a nucleic acid molecule encoding nARIA or biologically active variant thereof, in an amount sufficient to maintain synaptic connections in the  
10     subject and thereby treat neurdegeneration in the subject.
12. The method of claim 10 or 11, wherein the target cell is a somatic cell including a myocyte, a neuronal cell,  
15     a glandular cell or any postsynaptic cell.
13. The method of claim 10 or 11, wherein maintenance of the synaptic junction is accomplished in an individual having a neurological disorder involving abnormal synaptic connections.  
20
14. The method of claim 10, wherein the neurological disorder is a neuromuscular disorder or a neurodegenerative disease.  
25
15. The method of claim 10 or 11, wherein the nARIA polypeptide terminates with the amino acid sequence NQDPIAV (Seq ID No. \_\_) or the A-form of the cytoplamic domain of nARIA (Seq ID No. \_\_).  
30
16. The method of claim 10, wherein the neurological disorder is Alzheimer's Disease, Parkinson's disease, Turrets Syndrome, amyotrophic lateral sclerosis, Pick's disease, myasthenia gravis, or senility.  
35

17. A method for inducing neuronal regeneration which comprises contacting a target cell with a composition of nARIA and a pharmaceutically acceptable carrier to induce the formation of a synaptic junction between a neuron and a target cell.
18. The method of claim 17, wherein the target cell is a neuronal cell or a muscle cell.
19. A method for treating a neoplastic condition in a subject which comprises administering to the subject a pharmaceutically acceptable form of nARIA or a nARIA antagonist, which inhibits an interaction between nARIA and its receptor, in a sufficient amount over a sufficient time period to induce differentiation of neoplastic cells and thus treat the neoplastic condition.
20. A method for determining whether a compound is capable of modulating the binding of an nARIA polypeptide to its receptor, which comprises:
- (a) incubating the compound under suitable conditions with an appropriate nARIA polypeptide-affinity derivative or receptor-affinity derivative under appropriate conditions such that an affinity complex may form;
  - (b) measuring the amount of affinity complex formed so as to determine whether the compound is capable of modulating the binding of the nARIA polypeptide to its receptor.
21. The method of claim 20, wherein the affinity complex comprises an nARIA receptor bound to an affinity

derivative.

- 5 22. The method of claim 20, wherein the affinity complex comprises an nARIA polypeptide bound to an affinity derivative.
- 10 23. The method of claim 20, wherein measuring comprises binding of an antibody specific for nARIA to the affinity complex to measure the amount of affinity complex formed.
- 15 24. The method of claim 20, wherein the affinity derivative comprises sepharose, cellulose, plastic, glass, glass beads, or a streptavidin-coated plastic.
- 20 25. An assay for detecting neoplastic disease in a subject which comprises:  
a) obtaining a biological sample from the subject;  
b) contacting the sample with an agent that specifically binds to an expression product of a neuregulin gene or a neuregulin receptor;  
c) measuring the amount of agent bound by the sample;  
25 d) comparing the amount of agent bound measured in step c) with the the amount of agent bound by a standard normal sample, a higher amount bound by the sample from the subject being indicative of the presence of neoplastic disease in the subject.
- 30 26. The method of claim 25, wherein the neuregulin receptor is erbB2, erbB3 or erbB4.
- 35 27. The method of claim 25, wherein the agent specifically binds to an amino acid sequence of neuregulin which

09312795-151409

directs translocation to the nucleus.

28. The method of claim 25, wherein an expression product of a neuregulin gene comprises a neuregulin protein, an extracellular domain of a neuregulin protein, or a polypeptide encoded by the amino acid sequence shown in Figure 2 or 4.
29. The assay of claim 1, 2 or 25, wherein the agent is detectably labelled.

Add D'

Figure 1 shows the results of the 1000 randomizations. The mean values of the 1000 randomizations are shown in the top row of the figure. The mean values of the 1000 randomizations are shown in the top row of the figure. The mean values of the 1000 randomizations are shown in the top row of the figure.